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(54) Title: SURGICAL IMPLANT CONTAINING A RESORBABLE RADIOPAQUE MARKER

(57) Abstract

A surgical implant containing a resorbable radiopaque marker enables the position and/or orientation of the implant to be readily determined by x-ray or other radiographic technique following its surgical implantation in the body.

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SURGICAL IMPLANT CONTAINING A RESORBABLE RADIOPAQUE MARKER

BACKGROUND OF THE INVENTION

This invention is directed to a surgical implant, more particularly one containing a radiopaque marker which enables the position and/or orientation of the implant to be readily determined by x-ray or other radiographic technique following its surgical implantation in the body.

Osteoprosthetic implants are useful for repairing a variety of skeletal defects and irregularities. It may be necessary to confirm the location of an implant following its placement in the body. However, many osteoprosthetic implants are fabricated from materials, e.g., synthetic resins, that are transparent to radiographic imaging such as x-ray. Osteoprosthetic implants of this type have been provided with a radiopaque marker facilitating the determination of the position of the installed implant employing x-ray or other radiographic technique. See, e.g., U.S. Patent Nos. 3,829,904, 3,891,997, 3,922,726, 4,123,806, 4,224,698, 4,450,592, 5,405,402, 5,425,762, and 5,476,880. The radiopaque markers in the implants described in these patents takes the form of a metal wire formed from a biologically compatible metal such as stainless steel.

SUMMARY OF THE INVENTION

In accordance with the present invention, an implant for repairing skeletal defects and irregularities is provided which comprises an implant fabricated from a radiolucent material and possessing a resorbable radiopaque

marker, e.g., nondemineralized or partially demineralized bone particles. Unlike the metal wire radiopaque marker in the synthetic prostheses of the patents identified above, the implant of this invention has a radiopaque marker component which is resorbable in its entirety and may contribute to the healing of bone through natural processes.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The implant can be manufactured from any of several radiolucent resorbable or non-resorbable materials including demineralized bone sheet, particles, etc., collagen and collagen derivatives, plastic such as polyethylene cetabular cups.

In one embodiment of the present invention, the resorbable implant is manufactured from elongate demineralized bone particles as disclosed in U.S. Patent No. 5,507,813, the contents of which are incorporated herein by reference. According to the method described in U.S. Patent No. 5,507,813, elongate bone particles are obtained by milling from a section of whole bone, the particles are demineralized with acid in accordance with known and conventional procedures to provide substantially completely demineralized bone particles which are characteristically radiolucent and the bone particles are then formed into a shaped material possessing a definite geometrical configuration, e.g., a sheet possessing a square or rectangular shape. The sheet is formed by a wet-laying process the steps of which are as follows: slurrying a quantity of the demineralized elongate bone particles in a suitable liquid, e.g., water, organic protic solvent, aqueous solution such as physiological saline, etc., and optionally containing one or more biocompatible ingredients such as adhesives, fillers, plasticizers, flexibilizing agents, biostatic/biocidal agents, surface active agents,

medically/surgically useful substances, etc., applying the slurry to a porous support, e.g., a flat perforate sheet, mesh screen or three-dimensional mold, through which excess slurry liquid drains thereby providing a coherent, shaped wetted mass of demineralized bone particles and, optionally, drying the wetted mass. The sheet material thus formed is relatively rigid when dry and, upon contact with a biocompatible liquid, e.g., water, saline solution, etc., becomes pliable and flexible thus making it readily conformable to a desired bone repair site.

The radiopaque marker which is to be incorporated into the resorbable implant of this invention is advantageously provided as native bone obtained from either human or animal bone, e.g., by cutting, milling, grinding or other suitable technique. The radiopaque marker can also be partially demineralized bone, the extent of demineralization being not so great as to substantially impair its radiopaque character. For example, partially demineralized bone containing not less than about 50 weight percent of its original mineral content can be utilized as the radiopaque component of the implant of this invention. The radiopaque marker can also be a resorbable calcium-based mineral, e.g., hydroxyapatite, tricalcium phosphate, etc., or other resorbable inorganic material. The radiopaque marker is preferably provided in particulate form with an average particle size of from about 0.1 mm to about 10 mm and preferably from about 1 mm to about 5 mm. The radiopaque marker can be shaped in the form of spherical, quasi-spherical, cuboid, rectangular or any other shape which may be useful.

The radiopaque marker can be incorporated into the resorbable implant at any stage in the manufacture of the latter, e.g., in the case of a bone sheet manufactured in accordance with aforementioned U.S. Patent No. 5,507,813, by introduction into the slurry from which the bone sheet is made. The radiopaque marker can also be incorporated into the milled bone particles prior to their demineralization and formation into the bone sheet. However, as will be recognized, the radiopaque marker in this embodiment must be able to survive or be resistant to the demineralization process. In the case of a radiopaque marker made up of bone particles, by making such particles larger and/or thicker than the elongate bone particles intended for demineralization, it is possible to limit the extent of their demineralization so that they still contain sufficient inorganic matter to render them radiopaque while the elongate bone particles undergo complete, or nearly complete, demineralization. Another method of imparting resistance to demineralization to bone particles intended to function as the radiopaque marker is to coat the particles with a substance that is less susceptible to acid attack.

When incorporating the radiopaque marker into the resorbable implant, the marker can be arranged within the implant in a predetermined pattern, e.g., a geometric pattern such as a grid. This can be readily accomplished by use of a template placed over the implant during a processing step so that marker material that is poured or cast over the implant is only imbedded in desired areas. The usefulness of a predetermined pattern for the markers is to render the implant easily distinguishable from other surrounding structures in situ.

In the case of a resorbable implant which is fabricated from demineralized bone, application of the implant to the site of a bone defect, e.g., one resulting from injury, infection, malignancy or developmental malformation, leads to new bone ingrowth by one or more biological mechanisms such as osteogenesis, osteoconduction and/or osteoinduction or by one or more physical mechanisms such as providing a physical barrier to soft tissue ingrowth, presenting a support or scaffolding for new bone growth, etc.

Upon implantation of the implant into the body at a defect site, the implant can be viewed by using any of several known and conventional radiographic techniques such as x-ray imaging. In the case of x-ray imaging, the radiopaque marker is displayed on the exposed and developed x-ray film as white spots allowing the location and/or the orientation of the implant to be accurately determined.

The implant of this invention can be utilized in a wide variety of orthopaedic, neurosurgical and oral and maxillofacial surgical procedures such as the repair of simple and compound fractures and non-unions, external and internal fixations, joint reconstructions such as arthrodesis, general arthroplasty, cup arthroplasty of the hip, femoral and humeral head replacement, femoral head surface replacement and total joint replacement, repairs of the vertebral column including spinal fusion and internal fixation, tumor surgery, e.g. deficit filling, discectomy, laminectomy, excision of spinal cord tumors, anterior cervical and thoracic operations, repair of spinal injuries, scoliosis, lordosis and kyphosis treatments, intermaxillary fixation of fractures, mentoplasty, temporomandibular joint replacement, alveolar ridge augmentation and reconstruction,

inlay bone grafts, implant placement and revision, sinus lifts, etc. These materials can be sutured or stapled in place for anchoring purposes and serve in guided tissue regeneration or as barrier materials.

The following examples are illustrative of the resorbable implant of this invention.

EXAMPLE 1

A sheet fabricated from demineralized elongate bone particles is manufactured according to the method described in U.S. Patent No. 5,507,813. While the sheet is being wet-laid nondemineralized bone particles that have been classified to a predetermined range are added thereto. The mineralized particles are uniformly distributed within the wet sheet which is then subjected to the remaining manufacturing operations described in the aforesaid patent. The resultant flexible sheets are then cut into implant-sized pieces.

EXAMPLE 2

A small sheet from Example 1 is rehydrated and implanted into an animal at a calvarial defect site. The site is then sutured closed and the skull is x-rayed. The mineralized particles are displayed on the resultant x-ray film as white spots allowing the location of the implant to be precisely determined.

EXAMPLE 3

The nondemineralized bone particles in Example 1 can be incorporated into the wet-laid sheet in a regular pattern such as a grid with 5 mm spaces between particles. When the sheet processing is completed and a small sheet segment is rehydrated and implanted as in Example 2, the position/orientation of the sheet segment is more easily determined via x-ray imaging due to the regular pattern of the radiopaque nondemineralized particles.

Example 4

The nondemineralized particles of Example 1 can be distributed in a flowable osteogenic composition which is comprised of demineralized bone particles and an inert carrier such as glycerol.

WHAT IS CLAIMED IS:

1. A surgical implant for surgical implantation in the body, the implant being fabricated from radiolucent material and possessing a resorbable radiopaque marker.

2. The implant of Claim 1 wherein the radiolucent material is resorbable.

3. The implant of Claim 2 wherein the resorbable material is demineralized bone or collagen.

4. The implant of Claim 2 wherein the resorbable material is a flexible sheet of demineralized bone.

5. The implant of Claim 1 which possesses a definite geometrical configuration.

6. The implant of Claim 1 wherein the resorbable radiopaque marker comprises nondemineralized or partially demineralized bone particles.

7. The implant of Claim 6 wherein the nondemineralized or partially demineralized bone particles are selected from the group consisting of human and animal bone.

8. The implant of Claim 6 wherein the nondemineralized or partially demineralized bone particles are of a predetermined shape selected from the group consisting of spherical, quasi-spherical, cuboid, tube, fiber, spiral and rectangular.

9. The implant of Claim 6 wherein the partially demineralized bone particles contain not less than about 20 weight percent residual inorganic matter.

10. The implant of Claim 1 wherein the resorbable radiopaque marker is a calcium-based mineral selected from the group consisting of hydroxyapatite, tricalcium phosphate, fluorapatite and their mixtures.

11. The implant of Claim 1 wherein the resorbable radiopaque marker is arranged within the implant in accordance with a predetermined pattern.

12. The implant of Claim 11 wherein the predetermined pattern is a grid.

13. A method of determining the location and/or orientation of a surgical implant within a body which comprises:

a) surgically implanting within a body an implant fabricated from radiolucent material containing a resorbable radiopaque marker; and,

b) post-surgically determining the location and/or orientation of the implant by a radiographic technique.

14. The method of Claim 13 wherein radiolucent material is resorbable

15. The method of Claim 13 wherein the radiographic technique is x-ray imaging.

16. The method of Claim 13 wherein the radiopaque marker is arranged within the implant in accordance with a predetermined pattern.

17. The method of Claim 16 wherein the predetermined pattern is a grid.

INTERNATIONAL SEARCH REPORT

In. .ational Application No
PCT/US 97/16253

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61F2/02 A61L27/00 A61F2/30

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category '	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	DE 296 08 321 U (AESCULAP) 8 August 1996 see the whole document	1,2,10 3-5,11, 12
Y A	US 5 507 813 A (DOWD) 16 April 1996 cited in the application see abstract; claims 3,4,7	3-5 6-8
Y	US 4 795 463 A (GEROW) 3 January 1989 see figures 5,7; examples 4,5	11,12
X	US 5 108 399 A (EITENMULLER) 28 April 1992 see column 9, line 16 - line 31; claims 1,12	1,11
X	US 5 441 517 A (KENSEY) 15 August 1995 see claims 1,11	1

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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1

Date of the actual completion of the international search	Date of mailing of the international search report
12 December 1997	22.12.97

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Int. .ational Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 405 429 A (EURORESEARCH) 2 January 1991 see abstract; claims 1,10; figure	1-3,8
A	WO 94 21196 A (C.R. BARD) 29 September 1994 see abstract see page 4, line 21 - line 23	1,4
A	US 4 709 703 A (LAZAROW) 1 December 1987 see claim 3	1
A	US 4 123 806 A (AMSTUTZ) 7 November 1978 cited in the application see column 6, line 11 - line 17; figure 2	8,11
E	US 5 676 146 A (SCARBOROUGH) 14 October 1997 see the whole document	1-12

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 97/16253

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 13-17
because they relate to subject matter not required to be searched by this Authority, namely:

Method for treatment of the human body by surgery (cf. step (a) of claim 13): see PCT-Rule 39.1(iv)

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In. .ational Application No
PCT/US 97/16253

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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Information on patent family members

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PCT/US 97/16253

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